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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/866,801	05/30/2001	John W. Cherwonogrodzky	3929-3	5677

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/28/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/866,801	CHERWONOGRODZKY, JOHN W.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *1-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. Applicant's election with traverse of Group II, claims 13-29 in Paper No. 6 filed on October 17, 2001 is acknowledged. Group I, claims 1-12 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being to drawn a non-elected invention.

The traversal is on the grounds that Groups I-II are not independent and distinct, therefore the examination of the entire application does not constitute a serious burden. These arguments have been fully considered but are not found to be persuasive for the reasons below:

First, the classification system has no statutory recognition whether inventions are independent and distinct. For example, each class and subclass is comprised of numerous completely independent and distinct patented inventions.

Second, MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed and (2) a serious search and examination burden is placed on the examiner if restriction is not required.

The term "distinct" is defined to mean that two or more subjects as disclosed are related, for example as product and method of use, etc., but are capable of separate manufacture, use or sale as claimed, and are patentable over each (see MPEP 802.01). In the instant situation, the inventions of Groups I-II are drawn to distinct inventions which are separate products and methods capable of separate manufacture, use or sale as described in the previous Office Action.

Classification of the subject matter is merely one indication of the burdensome nature of the search. The literature search, particularly relevant in this art, is not co-extensive, because for example, Groups I and II are drawn to different products. Clearly different searches and issues are involved in the examination of each Group.

For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claim Objections

2. Claims 26 and 27 are objected to because they are drawn to a non-elected invention. The Applicant must amend the claims so that they are drawn to an elected invention.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

3. Claim 28 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 28 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for fungal and yeast cell culture supernatants, does not reasonably provide enablement for a vaccine comprising the fungal and yeast cell culture supernatants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claim 28 is drawn to the use of fungal or yeast culture supernatant as vaccines.

The specification fails to teach how to formulate the claimed vaccines. The term "vaccine" encompasses the ability of the specific antigen to induce protective immunity to a fungal or yeast infection or disease induction. The specification teaches that the claimed fungal or yeast supernatants containing antigenic components were used to vaccinate mice over a 10 week period. The specification merely states" that there was "considerable variation" of the response of mice to the different vaccinations cited in Table VI" (page 17).

The specification does not disclose how to formulate the fungal or yeast vaccine nor does the specification teach what dosages are required to treat a patient with a fungus or yeast infection? The specification does not provide substantive evidence that the claimed vaccines are capable of inducing protective immunity. This demonstration

is required for the skilled artisan to be able to use the claimed vaccines for their intended purpose of treating fungal or yeast infections. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed vaccines, i.e. would not be able to accurately predict if protective immunity has been induced. The specification further does not disclose what mode of administration can be used in regard to the vaccines to be capable of reaching the target organs necessary to treat a particular fungal or yeast infection. Therefore, it is unclear as to how to formulate a vaccine which will treat any fungal or yeast infection.

The ability to reasonably predict the capacity of a single bacterial immunogen or combinations of immunogens to induce protective immunity from *in vitro* antibody reactivity studies is problematic. Otcenasek et al *(Vet Med (Praha) April 1981 26(4): 193-202)* suggests that are theoretical problems of the nature and duration of immunity in regard to fungal vaccines (see the Abstract). Deepe, Jr., *(Clinical Microbiology Reviews, Oct. 1997, p.585-596)* teaches that historically vaccines used for coccidioidomycosis have failed. Deepe, Jr. teaches that fungal vaccines that can be formulated for human use are problematic. Deepe, Jr. teaches that concept of fungal vaccination for humans remains viable but has not attracted much attention because of the relatively low incidence of infection and the geographic distribution of several fungi compared to many viral and bacterial diseases (page 586). Deepe, Jr. teaches that one of the major problems exists with the formulation of fungal vaccines is that there are no motifs or canonical sequences exist that distinguish a protective fungal antigen from one that is not. Deepe, Jr. teaches that the concepts of how to determine if a gene or its

product can mediate protection must be take into consideration the method in which the immunogen is administered *in vivo*. Deepe, Jr., teaches that another potential problem exists in regard to using recombinant technology in establishing fungal vaccines. Deepe, Jr. teaches that production of peptides or small protein fragments may not be able to be expressed by prokaryotic expression systems because of size. Deepe , Jr. further teaches that fungal vaccination of immunocompromised host are problematic because most vaccines that elicit protective antibodies strictly rely on cellular immunity. Deepe, Jr. teaches vaccines that rely on cellular immunity may be none effective in an immunocompromised host (see page 593).

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to developing a fungal or yeast vaccine that would achieve a desire level of success when administered to a patient with a fungal or yeast infection that is capable of treating that fungal or yeast infection, 3) there are limited working examples which suggest the desired results of a successful

vaccine that is to treat any fungal or yeast infection, 4) the relative skill of those in the art is commonly recognized as quite high (post - doctoral level), and the lack of predictability in the field to which the invention pertains is recognized in the art as evidenced by the cited prior art.

In view of all of the above, in view of the lack of predictability in the art, it is determined that it would require undue experimentation to make and use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 18 is rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite "capable of". It is unclear as to what the applicant is referring? Thus, the metes and bounds of "capable of" cannot be ascertained. Clarification as to the meaning of this term is required.

6. Claim 24 is rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite "varying degrees". It is unclear as to what the applicant is referring? Thus, the metes and bounds of "varying degrees" cannot be ascertained. Clarification as to the meaning of this term is required.

7. Claim 25 is rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite "effective". It is unclear as to what the applicant is referring? Thus, the metes and bounds of "effective" cannot be ascertained. Clarification as to the meaning of this term is required.

8. Claim 26 is rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite "significant degree of". It is unclear as to what the applicant is referring? Thus, the metes and bounds of "significant degree of" cannot be ascertained. Clarification as to the meaning of this term is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The term "use of" is non-statutory. For Art purposes, the "use of " is beginning viewed as a method of using".

9. Claims 13-20, 22-24, 26 and 28-29 are rejected under 35 U.S.C. 102(b) as anticipated by Pasarell et al *(Journal of Clinical Microbiology, July 1990, p. 1655-1657).*

Claims 13-20, 22-24, 26 and 28-29 are drawn to a fungal or yeast cell culture supernatant as antigenic source for detecting levels of antibodies from a sample test subject.

Pasarell et al teach concentrated culture filtrate antigens that were obtained from the genera *Alternaria, Bipolaris, Curvularia, Dactylaria, Drechslera, Embellisia, Exserohilum, Fusarium, Helminthosporium, Microsporum, Scolecobasidium and Scopulariopsis.* Pasarell et al teach that the culture antigens were incubated and aerated on a rotating shaker (p. 1655, 2nd column). Pasarell et al teach that the concentrated culture filtrate antigens was used to immunize two New Zealand White female rabbits. Pasarell et al teach that an emulsion of 1 ml of each control antigen and 1 ml of Freund incomplete adjuvant was injected intramuscularly into the New Zealand rabbits. *Alternaria, Dactylaria, Drechslera, Embellisia, Fusarium, Micosporum, Scolecobasisum and Scolecobasidium and Scopulariopsis* did not have common antigens when tested against the antisera. Antigens of *Helminthosporium* only reacted with its own sera and there were no cross-reactions with any other antigens tested (p. 1656, 1st column). Pasarell et al teach that antisera prepared from *E. rostratum* recognized antigens prepared from *E. holmii.* Pasarell et al teach that a similar result was observed with antisera prepare from *E. mcginnisii* and *E. longirostratum.* Pasarell et al that common antigens are shared between the genera of *Bipolaris* and *Curvularia* (p. 1656). The process limitation of the supernatant being prepared and used at 20°C is

a matter of design choice. Although the reference appears to disclose the same cell culture supernatant claimed by the Applicants, the reference does not disclose the cell culture supernatant being prepared at the same temperature as the claimed process. However, the production of a cell culture supernatant by a particular process does not impart novelty or unobviousness to a cell culture supernatant when the same cell culture supernatant is taught in the prior art. This particularly true when properties of the cell culture supernatant are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972). The fungal or yeast culture of Pasarell, et al appears to be the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's fungal or yeast culture supernatant with the fungal or yeast culture supernatant of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (i.e.,that the fungal or yeast culture supernatant of the prior art does not possess the same material structural and functional characteristics of the claimed fungal or yeast culture supernatant). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

10. Claims 13-22, 24-25 and 29 are rejected under 35 U.S.C. 102(b) as anticipated by Calera et al *(Infection and Immunity, June 1994, p. 2322-2333).*

Claims 13-22, 24-25 and 29 are drawn to a fungal or yeast cell culture supernatant as antigenic source for detecting levels of antibodies from a sample test subject.

Calera et al teach cell culture supernatants obtained from *Aspergillus* (see the Abstract and page 2324). Calera teach that *Aspergillus nidulans* antigens elicit antibodies in rabbits. Calera et al teach that the *Aspergillus nidulans* antigens cross-reacted with antigens from *A. fumigatus, A. flavus, A. terreus, A. clavatus* and *A. niger* (p. 2331). Calera et al teach that screening a battery of 10 selected human serum samples from patients with aspergilloma or invasive aspergillosis demonstrated that two antigens from stationary-phase culture supernatants were consistently reactive (see the Abstract). It would be inherent that the *Aspergillus* antigens would be effective in detecting aflatoxins since aflatoxins are obtained from microorganisms of the genera *Aspergillus*. The process limitation of the supernatant being prepared and used at 20°C is a matter of design choice. Although the reference appears to disclose the same cell culture supernatant claimed by the Applicants, the reference does not disclose the cell culture supernatant being prepared at the same temperature as the claimed process. However, the production of a cell culture supernatant by a particular process does not impart novelty or unobviousness to a cell culture supernatant when the same cell culture supernatant is taught in the prior art. This particularly true when properties of the cell culture supernatant are not changed by the process in an unexpected manner.

See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972). It would be inherent that the reference of the prior art would detect aflatoxins. The fungal or yeast culture of Calera, et al appears to be the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's fungal or yeast culture supernatant with the fungal or yeast culture supernatant of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (i.e.,that the fungal or yeast culture supernatant of the prior art does not possess the same material structural and functional characteristics of the claimed fungal or yeast culture supernatant). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

11. Claims 13-18, 27 and 29 are rejected under 35 U.S.C. 102(a) as anticipated by Barros et al *(Rev. inst. Med. Trop. S. Paulo 41 (6): 343-350, November-December 1999).*

Claims 13-18, 27 and 29 are drawn to the fungal cell culture supernatant as antigenic source for detecting level of antibodies from a sample test subject.

Barros et al teach antigenic preparations from *Cladophilophora (Cladosporium) carrionii* (see the Abstract and page 344). Barros et al also teach that partial chemical characterization of the antigenic preparations were obtained by determination of the levels of total lipids, protein and carbohydrates (see the Abstract and page 345, Tables

1-4). It is well known that *Cladosporium* can give "false positive" results when in diagnostic assays as evidenced by Malling et al *(Allergy, January, 41(1):57-67)*. The process limitation of the supernatant being prepared and used at 20°C is a matter of design choice. Although the reference appears to disclose the same cell culture supernatant claimed by the Applicants, the reference does not disclose the cell culture supernatant being prepared at the same temperature as the claimed process. However, the production of a cell culture supernatant by a particular process does not impart novelty or unobviousness to a cell culture supernatant when the same cell culture supernatant is taught in the prior art. This particularly true when properties of the cell culture supernatant are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972). The fungal or yeast culture of Barros, et al appears to be the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's fungal or yeast culture supernatant with the fungal or yeast culture supernatant of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (i.e.,that the fungal or yeast culture supernatant of the prior art does not possess the same material structural and functional characteristics of the claimed fungal or yeast culture supernatant). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

12. Claims 13-18, 25 and 28-29 are rejected under 35 U.S.C. 102(a) as anticipated by Taylor et al, *(J. Allergy Clin. Immunol., March 1988, Vol. 81 No. 3, p. 548-557).*

Claims 13-18, 25 and 28-29 are drawn to the fungal cell culture supernatant as antigenic source for detecting level of antibodies from a sample test subject.

Taylor et al teach antigenic cultures of *Aspergillus fumigatus* which were grown at 25°C and shaken in either 20 ml of Coca's solution or 20 ml of HBSS (page 549). Taylor et al teach that rabbits were immunized with the formalin-fixed conidia, resuspended in 1 ml of saline and emulsified in 3 ml of Freund's incomplete adjuvant (page 549). The fungal or yeast culture of Taylor, et al appears to be the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's fungal or yeast culture supernatant with the fungal or yeast culture supernatant of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (i.e.,that the fungal or yeast culture supernatant of the prior art does not possess the same material structural and functional characteristics of the claimed fungal or yeast culture supernatant). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Pertinent Prior Art

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure *(Murali et al, Chest, Vol. 106, No. 2, August 1994).*

Status of Claims

14. No claims are allowed.

Conclusion

15. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
January 26, 2001

JAMES O. WILSON
PRIMARY EXAMINER
GROUP 1600